

or a pharmaceutically acceptable salt thereof, wherein:

*Sub E1*

R<sub>1</sub> and R<sub>3</sub> are independently selected from hydrogen, halogen, cyano, C<sub>1-6</sub> alkyl, C<sub>2-6</sub>alkenyl, C<sub>2-6</sub>alkynyl, (C<sub>3-7</sub>cycloalkyl<sub>1</sub>)C<sub>1-4</sub>alkyl, (C<sub>3-7</sub>cycloalkyl<sub>1</sub>)C<sub>2-4</sub>alkenyl, (C<sub>3-7</sub>cycloalkyl<sub>1</sub>) C<sub>2-4</sub>alkynyl, -O(C<sub>3-7</sub>cycloalkyl<sub>1</sub>)C<sub>1-4</sub>alkyl, -O(C<sub>3-7</sub>cycloalkyl<sub>1</sub>)C<sub>2-4</sub>alkenyl, -O(C<sub>3-7</sub>cycloalkyl<sub>1</sub>) C<sub>2-4</sub>alkynyl, halo(C<sub>1-6</sub>)alkyl, haloC<sub>2-6</sub>alkenyl, haloC<sub>2-6</sub>alkynyl, -O(halo(C<sub>1-6</sub>)alkyl), -O(halo(C<sub>2-6</sub>)alkenyl), -O(halo(C<sub>2-6</sub>)alkynyl), -O(C<sub>1-6</sub>alkyl), -O(C<sub>2-6</sub>alkenyl), -O(C<sub>2-6</sub>alkynyl), S(O)<sub>n</sub>(C<sub>1-6</sub>alkyl), S(O)<sub>n</sub>(C<sub>2-6</sub>alkenyl), and S(O)<sub>n</sub>(C<sub>2-6</sub>alkynyl),

where each alkyl, or alkenyl is independently straight, branched, or cyclic, and each alkynyl is straight or branched, and is optionally substituted with one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, C<sub>1-4</sub>alkoxy, amino, and mono- or di(C<sub>1-4</sub>)alkylamino,

and

where each C<sub>3-7</sub>cycloalkyl<sub>1</sub> is optionally substituted by one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, C<sub>1-4</sub>alkoxy, amino, and mono- or di(C<sub>1-4</sub>)alkylamino,

with the proviso that not both R<sub>1</sub> and R<sub>3</sub> are hydrogen;

R<sub>2</sub> is selected from the group consisting of -XR<sub>A</sub> and Y; and

Ar is selected from the group consisting of phenyl, naphthyl, pyridyl, pyrimidinyl, pyridizinyl, and thiophenyl, each of which is mono-, di-, or tri-substituted with R<sub>C</sub>;

R<sub>A</sub> and R<sub>B</sub>, which may be the same or different, are independently selected at each occurrence from:

hydrogen, straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, (cycloalkyl)alkyl groups consisting of 4 to 11 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups

consisting of 2 to 8 carbon atoms, each of which may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, cyano, amino, C<sub>1-6</sub>alkoxy, -NH(C<sub>1-6</sub>alkyl), -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl), -NHC(=O)(C<sub>1-6</sub>alkyl), -N(C<sub>1-6</sub>alkyl)C(=O)(C<sub>1-6</sub>alkyl), -NHS(O)<sub>n</sub>(C<sub>1-6</sub>alkyl), -S(O)<sub>n</sub>(C<sub>1-6</sub>alkyl), -S(O)<sub>n</sub>NH(C<sub>1-6</sub>alkyl), -S(O)<sub>n</sub>N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl), and Z;

R<sub>C</sub> is independently selected at each occurrence from halogen, cyano, halo(C<sub>1-6</sub>)alkyl, halo(C<sub>1-6</sub>)alkoxy, hydroxy, amino, C<sub>1-6</sub>alkyl substituted with 0-2 R<sub>D</sub>, C<sub>2-6</sub> alkenyl substituted with 0-2 R<sub>D</sub>, C<sub>2-6</sub>alkynyl substituted with 0-2 R<sub>D</sub>, C<sub>3-7</sub>cycloalkyl substituted with 0-2 R<sub>D</sub>, (C<sub>3-7</sub>cycloalkyl)C<sub>1-4</sub>alkyl substituted with 0-2 R<sub>D</sub>, C<sub>1-6</sub>alkoxy substituted with 0-2 R<sub>D</sub>, -NH(C<sub>1-6</sub>alkyl) substituted with 0-2 R<sub>D</sub>, -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl) each C<sub>1-6</sub>alkyl independently substituted with 0-2 R<sub>D</sub>, -XR<sub>A</sub>, and Y;

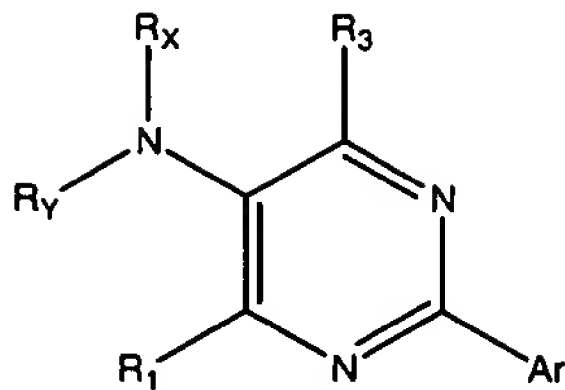
R<sub>D</sub> is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, amino, C<sub>1-4</sub>alkyl, -O(C<sub>1-4</sub>alkyl), -NH(C<sub>1-4</sub>alkyl), -N(C<sub>1-4</sub>alkyl)(C<sub>1-4</sub>alkyl), -S(O)<sub>n</sub>(alkyl), halo(C<sub>1-4</sub>)alkyl, halo(C<sub>1-4</sub>)alkoxy, CO(C<sub>1-4</sub>alkyl), CONH(C<sub>1-4</sub>alkyl), CON(C<sub>1-4</sub>alkyl)(C<sub>1-4</sub>alkyl), -XR<sub>A</sub>, and Y;

X is independently selected at each occurrence from the group consisting of -CH<sub>2</sub>-, -CHR<sub>B</sub>-, -O-, -C(=O)-, -C(=O)O-, -S(O)<sub>n</sub>-, -NH-, -NR<sub>B</sub>-, -C(=O)NH-, -C(=O)NR<sub>B</sub>-, -S(O)<sub>n</sub>NH-, -S(O)<sub>n</sub>NR<sub>B</sub>-, -OC(=S)S-, -NHC(=O)-, -NR<sub>B</sub>C(=O)-, -NHS(O)<sub>n</sub>-, -OSiH<sub>n</sub>(C<sub>1-4</sub>alkyl)<sub>2-n</sub>-, and -NR<sub>B</sub>S(O)<sub>n</sub>-;

Y and Z are independently selected at each occurrence from: 3- to 7-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, cyano, C<sub>1-4</sub>alkyl, -O(C<sub>1-4</sub>alkyl), -NH(C<sub>1-4</sub>alkyl), -N(C<sub>1-4</sub>alkyl)(C<sub>1-4</sub>alkyl), and -S(O)<sub>n</sub>(alkyl),

said 3- to 7-membered heterocyclic groups containing one or more heteroatom(s) independently selected from N, O, and S, with the point of attachment being either carbon or nitrogen; and

n is independently selected at each occurrence from 0, 1, and 2.



### Formula A

or a pharmaceutically acceptable salt thereof, wherein:

$R_X$  and  $R_Y$  are the same or different and are independently selected from:

- a) hydrogen,
- b)  $-(C=O)alkyl_A$ , wherein  $alkyl_A$  is a straight or branched alkyl group having from 1 to 8 carbon atoms;
- c) straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, cycloalkyl(alkyl) groups consisting of 4 to 11 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms, each of which may be further substituted with one or more substituent(s) independently selected from:
- i) hydroxy, halogen, amino, cyano,  $-O(C_{1-4}alkyl)$ ,  $-NH(C_{1-4}alkyl)$ , and  $-NH(C_{1-4}alkyl)(C_{1-4}alkyl)$ , and
  - ii) 3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be substituted with one or more substituents independently selected from halogen, halo( $C_{1-4}$ )alkyl, halo( $C_{1-4}$ )alkoxy, oxo, hydroxy, amino,  $C_{1-4}alkyl$ ,  $-O(C_{1-4}alkyl)$ ,  $-NH(C_{1-4}alkyl)$ ,  $-N(C_{1-4}alkyl)(C_{1-4}alkyl)$ , and  $-S(O)_n(alkyl)$ , wherein said 3- to 7-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S, with the point of attachment being either carbon or nitrogen,

R<sub>1</sub> and R<sub>3</sub> are independently selected from hydrogen, halogen, cyano, C<sub>1-6</sub> alkyl, C<sub>2-6</sub>alkenyl, C<sub>2-6</sub>alkynyl, (C<sub>3-7</sub>cycloalkyl)<sub>1</sub>C<sub>1-4</sub>alkyl, (C<sub>3-7</sub>cycloalkyl)<sub>1</sub>C<sub>2-4</sub>alkenyl, (C<sub>3-7</sub>cycloalkyl)<sub>1</sub> C<sub>2-4</sub>alkynyl, -O(C<sub>3-7</sub>cycloalkyl)<sub>1</sub>C<sub>1-4</sub>alkyl, -O(C<sub>3-7</sub>cycloalkyl)<sub>1</sub>C<sub>2-4</sub>alkenyl, -O(C<sub>3-</sub>

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~~cycloalkyl<sub>1</sub>) C<sub>2-4</sub>alkynyl, halo(C<sub>1-6</sub>)alkyl, haloC<sub>2-6</sub>alkenyl, haloC<sub>2-6</sub>alkynyl, -O(halo(C<sub>1-6</sub>)alkyl), -O(halo(C<sub>2-6</sub>)alkenyl), -O(halo(C<sub>2-6</sub>)alkynyl), -O(C<sub>1-6</sub>alkyl), -O(C<sub>2-6</sub>alkenyl), -O(C<sub>2-6</sub>alkynyl), S(O)<sub>n</sub>(C<sub>1-6</sub>alkyl), S(O)<sub>n</sub>(C<sub>2-6</sub>alkenyl), and S(O)<sub>n</sub>(C<sub>2-6</sub>alkynyl),~~

~~where each alkyl, or alkenyl is independently straight, branched, or cyclic, and each alkynyl is straight or branched, and is optionally substituted by one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, C<sub>1-4</sub>alkoxy, amino, and mono- or di(C<sub>1-4</sub>)alkylamino,~~

~~and~~

~~where said C<sub>3-7</sub>cycloalkyl<sub>1</sub> is optionally substituted by one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, C<sub>1-4</sub>alkoxy, amino, and mono- or di(C<sub>1-4</sub>)alkylamino~~

~~with the proviso that not both R<sub>1</sub> and R<sub>3</sub> are hydrogen;~~

~~Ar is selected from the group consisting of phenyl, naphthyl, pyridyl, pyrimidinyl, and thiophenyl, each of which is mono-, di-, or tri-substituted with R<sub>C</sub>;~~

~~R<sub>A</sub> and R<sub>B</sub>, which may be the same or different, are independently selected at each occurrence from the group consisting of:~~

~~hydrogen, straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, (cycloalkyl)alkyl groups consisting of 4 to 11 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, and straight or branched alkynyl groups consisting of 2 to 8 carbon atoms, each of which may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, nitro, cyano, C<sub>1-6</sub>alkoxy, -NH(C<sub>1-6</sub>alkyl), -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl), -NHC(=O)(C<sub>1-6</sub>alkyl), -N(C<sub>1-6</sub>alkyl)C(=O)(C<sub>1-6</sub>alkyl), -NHS(O)<sub>n</sub>(C<sub>1-6</sub>alkyl), -S(O)<sub>n</sub>(C<sub>1-6</sub>alkyl), -S(O)<sub>n</sub>NH(C<sub>1-6</sub>alkyl), -S(O)<sub>n</sub>N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl), and Z;~~

~~R<sub>C</sub> is independently selected at each occurrence from halogen, cyano, halo(C<sub>1-6</sub>)alkyl, halo(C<sub>1-6</sub>)alkoxy, hydroxy, amino, and C<sub>1-6</sub>alkyl substituted with 0-2 R<sub>D</sub>, C<sub>2-6</sub>alkenyl substituted with 0-2 R<sub>D</sub>, C<sub>2-6</sub>alkynyl substituted with 0-2 R<sub>D</sub>, C<sub>3-7</sub>cycloalkyl substituted with 0-2 R<sub>D</sub>, (C<sub>3-7</sub>cycloalkyl)C<sub>1-4</sub>alkyl substituted with 0-2 R<sub>D</sub>, C<sub>1-6</sub>alkoxy substituted with 0-2 R<sub>D</sub>, -NH(C<sub>1-6</sub>alkyl) substituted with 0-2 R<sub>D</sub>, -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl) each C<sub>1-4</sub>alkyl~~

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independently substituted with 0-2  $R_D$ ,  $-XR_A$ , and Y, with the proviso that at least one of the positions ortho or para to the point of attachment of Ar to the pyrimidine ring shown in Formula A is substituted;

$R_D$  is independently selected at each occurrence the group consisting of halogen, hydroxy, cyano,  $C_{1-4}$ alkyl,  $-O(C_{1-4}$ alkyl),  $-NH(C_{1-4}$ alkyl),  $-N(C_{1-4}$ alkyl)( $C_{1-4}$ alkyl),  $-S(O)_n$ (alkyl) halo( $C_{1-4}$ alkyl), halo( $C_{1-4}$ )alkoxy,  $CO(C_{1-4}$ alkyl),  $CONH(C_{1-4}$ alkyl),  $CON(C_{1-4}$ alkyl)( $C_{1-4}$ alkyl),  $-XR_A$ , and Y;

Sub E1  
X is independently selected at each occurrence from the group consisting of  $-CH_2-$ ,  $-CHR_B-$ ,  $-O-$ ,  $-C(=O)-$ ,  $-C(=O)O-$ ,  $-S(O)_n-$ ,  $-NH-$ ,  $-NR_B-$ ,  $-C(=O)NH-$ ,  $-C(=O)NR_B-$ ,  $-S(O)_nNH-$ ,  $-S(O)_nNR_B-$ ,  $-OC(=S)S-$ ,  $-NHC(=O)-$ ,  $-NR_BC(=O)-$ ,  $-NHS(O)_n-$ ,  $-OSiH_n(C_{1-4}\text{-alkyl})_{2-n}-$ , and  $-NR_BS(O)_n-$ ;

Y and Z are independently selected at each occurrence from the group consisting of: 3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino,  $C_{1-4}$ alkyl,  $-O(C_{1-4}$ alkyl),  $-NH(C_{1-4}$ alkyl),  $-N(C_{1-4}$ alkyl)( $C_{1-4}$ alkyl), and  $-S(O)_n$ (alkyl); and

n is 0, 1, or 2.

10. (thrice amended) A compound or salt according to Claim 9, wherein:

$R_X$  and  $R_Y$  are the same or different and are independently selected from:

- a)  $-(C=O)alkyl_A$ , wherein  $alkyl_A$  is a straight or branched alkyl group having from 1 to 8 carbon atoms;
- b) straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, (cycloalkyl)alkyl groups consisting of 4 to 12 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms, each of which may be further substituted with one or more substituent(s) independently selected from:
  - i) hydroxy, halogen, amino, cyano,  $-O(C_{1-4}alkyl)$ ,  $-NH(C_{1-4}alkyl)$ , and  $-NH(C_{1-4}alkyl)(C_{1-4}alkyl)$ , and

ii) 3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be substituted with one or more substituents independently selected from halogen, halo(C<sub>1-4</sub>)alkyl, halo(C<sub>1-4</sub>)alkoxy, oxo, hydroxy, amino, C<sub>1-4</sub>alkyl, -O(C<sub>1-4</sub>alkyl), -NH(C<sub>1-4</sub>alkyl), -N(C<sub>1-4</sub>alkyl)(C<sub>1-4</sub>alkyl), and -S(O)<sub>n</sub>(alkyl), wherein said 3- to 7-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S, with the point of attachment being either carbon or nitrogen,

0<sup>2</sup>  
R<sub>1</sub> and R<sub>3</sub> are independently selected from hydrogen, halogen, cyano, C<sub>1-6</sub> alkyl, C<sub>2-6</sub>alkenyl, C<sub>2-6</sub>alkynyl, (C<sub>3-7</sub>cycloalkyl<sub>1</sub>)C<sub>1-4</sub>alkyl, (C<sub>3-7</sub>cycloalkyl<sub>1</sub>)C<sub>2-4</sub>alkenyl, (C<sub>3-7</sub>cycloalkyl<sub>1</sub>) C<sub>2-4</sub>alkynyl, -O(C<sub>3-7</sub>cycloalkyl<sub>1</sub>)C<sub>1-4</sub>alkyl, -O(C<sub>3-7</sub>cycloalkyl<sub>1</sub>)C<sub>2-4</sub>alkenyl, -O(C<sub>3-7</sub>cycloalkyl<sub>1</sub>) C<sub>2-4</sub>alkynyl, halo(C<sub>1-6</sub>)alkyl, haloC<sub>2-6</sub>alkenyl, haloC<sub>2-6</sub>alkynyl, -O(halo(C<sub>1-6</sub>)alkyl), -O(halo(C<sub>2-6</sub>)alkenyl), -O(halo(C<sub>2-6</sub>)alkynyl), -O(C<sub>1-6</sub>alkyl), -O(C<sub>2-6</sub>alkenyl), and -O(C<sub>2-6</sub>alkynyl),

where each alkyl, or alkenyl is independently straight, branched, or cyclic, and each alkynyl is straight or branched, and is optionally substituted by one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, C<sub>1-4</sub>alkoxy, amino, and mono- or di(C<sub>1-4</sub>)alkylamino,

and

where said C<sub>3-7</sub>cycloalkyl<sub>1</sub> is optionally substituted by one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, C<sub>1-4</sub>alkoxy, amino, and mono- or di(C<sub>1-4</sub>)alkylamino

Ar is phenyl, which is mono-, di-, or tri-substituted with R<sub>C</sub>;

R<sub>A</sub> and R<sub>B</sub>, which may be the same or different, are independently selected at each occurrence from the group consisting of:

hydrogen, straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, (cycloalkyl)alkyl groups consisting of 4 to 11 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, and straight or branched alkynyl groups consisting of 2 to 8 carbon atoms, each of which may be further substituted with one or



more substituent(s) independently selected from oxo, hydroxy, halogen, nitro, cyano, C<sub>1-6</sub>alkoxy, -NH(C<sub>1-6</sub>alkyl), -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl), -NHC(=O)(C<sub>1-6</sub>alkyl), -N(C<sub>1-6</sub>alkyl)C(=O)(C<sub>1-6</sub>alkyl), and Z;

*D<sup>2</sup>*  
R<sub>C</sub> is independently selected at each occurrence from halogen, cyano, halo(C<sub>1-6</sub>)alkyl, halo(C<sub>1-6</sub>)alkoxy, hydroxy, amino, and C<sub>1-6</sub>alkyl substituted with 0-2 R<sub>D</sub>, C<sub>2-6</sub> alkenyl substituted with 0-2 R<sub>D</sub>, C<sub>2-6</sub>alkynyl substituted with 0-2 R<sub>D</sub>, C<sub>3-7</sub>cycloalkyl substituted with 0-2 R<sub>D</sub>, (C<sub>3-7</sub>cycloalkyl)C<sub>1-4</sub>alkyl substituted with 0-2 R<sub>D</sub>, C<sub>1-6</sub>alkoxy substituted with 0-2 R<sub>D</sub>, -NH(C<sub>1-6</sub>alkyl) substituted with 0-2 R<sub>D</sub>, -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl) each C<sub>1-4</sub>alkyl independently substituted with 0-2 R<sub>D</sub>, -XR<sub>A</sub>, and Y, with the proviso that at least one of the positions ortho or para to the point of attachment of Ar to the pyrimidine ring shown in Formula A is substituted;

R<sub>D</sub> is independently selected at each occurrence the group consisting of halogen, hydroxy, cyano, C<sub>1-4</sub>alkyl, -O(C<sub>1-4</sub>alkyl), -NH(C<sub>1-4</sub>alkyl), -N(C<sub>1-4</sub>alkyl)(C<sub>1-4</sub>alkyl), halo(C<sub>1-4</sub>)alkyl, halo(C<sub>1-4</sub>)alkoxy, CO(C<sub>1-4</sub>alkyl), CONH(C<sub>1-4</sub>alkyl), CON(C<sub>1-4</sub>alkyl)(C<sub>1-4</sub>alkyl), -XR<sub>A</sub>, and Y;

X is independently selected at each occurrence from the group consisting of -CH<sub>2</sub>-, -CHR<sub>B</sub>-, -O-, -C(=O)-, -C(=O)O-, -NH-, -NR<sub>B</sub>-, -C(=O)NH-, -C(=O)NR<sub>B</sub>-, -NHC(=O)-, and -NR<sub>B</sub>C(=O)-;

Y and Z are independently selected at each occurrence from the group consisting of: 3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, C<sub>1-4</sub>alkyl, -O(C<sub>1-4</sub>alkyl), -NH(C<sub>1-4</sub>alkyl), and -N(C<sub>1-4</sub>alkyl)(C<sub>1-4</sub>alkyl); and

n is 0, 1, or 2.

13. (thrice amended) A compound or salt according to claim 9, wherein:

*03*  
Ar is phenyl mono-, di-, or tri-substituted with R<sub>C</sub>,

*5-6*  
*E1*  
R<sub>X</sub> and R<sub>Y</sub>, which may be the same or different, are independently selected at each occurrence from

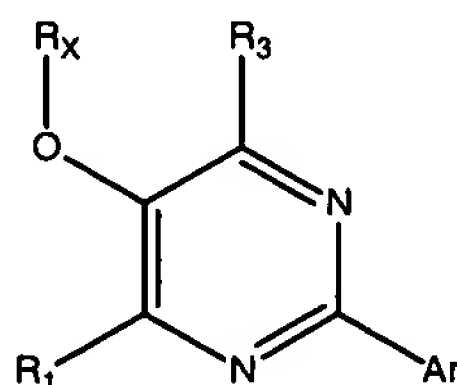
straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, (cycloalkyl)alkyl groups consisting of 4 to 11 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms; and

03 R<sub>1</sub> and R<sub>3</sub> are independently selected from the group consisting of hydrogen, halogen, C<sub>1-4</sub>alkoxy, halo(C<sub>1-4</sub>)alkyl, (halo(C<sub>1-4</sub>)alkoxy,

C<sub>1-6</sub>alkyl, which C<sub>1-6</sub>alkyl is unsubstituted or substituted by one to three substituents independently selected from hydroxy, oxo, cyano, C<sub>1-4</sub>alkoxy, amino, and mono- or di(C<sub>1-4</sub>)alkylamino,

(C<sub>3-7</sub>cycloalkyl)C<sub>1-4</sub>alkyl, which (C<sub>3-7</sub>cycloalkyl)C<sub>1-4</sub>alkyl is unsubstituted or substituted by one to three substituents independently selected from hydroxy, oxo, cyano, C<sub>1-4</sub>alkoxy, amino, and mono- or di(C<sub>1-4</sub>)alkylamino.

15. (thrice amended) A compound or salt according to the formula



DA  
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El  
wherein:

R<sub>x</sub> is chosen from

straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, (cycloalkyl)alkyl groups consisting of 4 to 12 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms, each of which may be further substituted with one or more substituent(s) independently selected from:

(a) hydroxy, halogen, amino, cyano, -O(C<sub>1-4</sub>alkyl), -NH(C<sub>1-4</sub>alkyl), and -NH(C<sub>1-4</sub>alkyl)(C<sub>1-4</sub>alkyl), and



(b) 3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be substituted with one or more substituents selected from halogen, halo(C<sub>1-4</sub>)alkyl, oxo, hydroxy, amino, C<sub>1-4</sub>alkyl, -O(C<sub>1-4</sub>alkyl), -NH(C<sub>1-4</sub>alkyl), -N(C<sub>1-4</sub>alkyl)(C<sub>1-4</sub>alkyl), wherein said 3- to 7-membered heterocyclic groups contain one or more heteroatom(s) selected from N, O, and S, with the point of attachment being either carbon or nitrogen;

R<sub>1</sub> and R<sub>3</sub> are independently selected from hydrogen, halogen, cyano, C<sub>1-6</sub> alkyl, C<sub>2-6</sub>alkenyl, C<sub>2-6</sub>alkynyl, (C<sub>3-7</sub>cycloalkyl<sub>1</sub>)C<sub>1-4</sub>alkyl, (C<sub>3-7</sub>cycloalkyl<sub>1</sub>)C<sub>2-4</sub>alkenyl, (C<sub>3-7</sub>cycloalkyl<sub>1</sub>) C<sub>2-4</sub>alkynyl, -O(C<sub>3-7</sub>cycloalkyl<sub>1</sub>)C<sub>1-4</sub>alkyl, -O(C<sub>3-7</sub>cycloalkyl<sub>1</sub>)C<sub>2-4</sub>alkenyl, -O(C<sub>3-7</sub>cycloalkyl<sub>1</sub>) C<sub>2-4</sub>alkynyl, halo(C<sub>1-6</sub>)alkyl, haloC<sub>2-6</sub>alkenyl, haloC<sub>2-6</sub>alkynyl, -O(halo(C<sub>1-6</sub>)alkyl), -O(halo(C<sub>2-6</sub>)alkenyl), -O(halo(C<sub>2-6</sub>)alkynyl), -O(C<sub>1-6</sub>alkyl), -O(C<sub>2-6</sub>alkenyl), -O(C<sub>2-6</sub>alkynyl), S(O)<sub>n</sub>(C<sub>1-6</sub>alkyl), S(O)<sub>n</sub>(C<sub>2-6</sub>alkenyl), and S(O)<sub>n</sub>(C<sub>2-6</sub>alkynyl),

where each alkyl, or alkenyl is independently straight, branched, or cyclic, and each alkynyl is straight or branched, and is optionally substituted by one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, C<sub>1-4</sub>alkoxy, amino, and mono- or di(C<sub>1-4</sub>)alkylamino,

and

where said C<sub>3-7</sub>cycloalkyl<sub>1</sub> is optionally substituted by one or more substituents independently chosen from halogen, hydroxy, oxo, cyano, C<sub>1-4</sub>alkoxy, amino, and mono- or di(C<sub>1-4</sub>)alkylamino

with the proviso that not both R<sub>1</sub> and R<sub>3</sub> are hydrogen;

Ar is selected from the group consisting of phenyl, naphthyl, pyridyl, pyrimidinyl, and thiophenyl, each of which is mono-, di-, or tri-substituted with R<sub>C</sub>;

R<sub>A</sub> and R<sub>B</sub>, which may be the same or different, are independently selected at each occurrence from the group consisting of:

hydrogen, straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, (cycloalkyl)alkyl groups consisting of 4 to 11 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, and straight or branched alkynyl groups consisting of 2 to 8 carbon atoms, each of which may be further substituted with one or

more substituent(s) independently selected from oxo, hydroxy, halogen, nitro, cyano, C<sub>1-6</sub>alkoxy, -NH(C<sub>1-6</sub>alkyl), -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl), -NHC(=O)(C<sub>1-6</sub>alkyl), -N(C<sub>1-6</sub>alkyl)C(=O)(C<sub>1-6</sub>alkyl), -NHS(O)<sub>n</sub>(C<sub>1-6</sub>alkyl), -S(O)<sub>n</sub>(C<sub>1-6</sub>alkyl), -S(O)<sub>n</sub>NH(C<sub>1-6</sub>alkyl), -S(O)<sub>n</sub>N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl), and Z;

*Sub E1*  
*pk*  
R<sub>C</sub> is independently selected at each occurrence from halogen, cyano, halo(C<sub>1-6</sub>)alkyl, halo(C<sub>1-6</sub>)alkoxy, hydroxy, amino, and C<sub>1-6</sub>alkyl substituted with 0-2 R<sub>D</sub>, C<sub>2-6</sub> alkenyl substituted with 0-2 R<sub>D</sub>, C<sub>2-6</sub>alkynyl substituted with 0-2 R<sub>D</sub>, C<sub>3-7</sub>cycloalkyl substituted with 0-2 R<sub>D</sub>, (C<sub>3-7</sub>cycloalkyl)C<sub>1-4</sub>alkyl substituted with 0-2 R<sub>D</sub>, C<sub>1-6</sub>alkoxy substituted with 0-2 R<sub>D</sub>, -NH(C<sub>1-6</sub>alkyl) substituted with 0-2 R<sub>D</sub>, -N(C<sub>1-6</sub>alkyl)(C<sub>1-6</sub>alkyl) each C<sub>1-4</sub>alkyl independently substituted with 0-2 R<sub>D</sub>, -XR<sub>A</sub>, and Y, with the proviso that at least one of the positions ortho or para to the point of attachment of Ar to the pyrimidine ring shown in Formula A is substituted;

R<sub>D</sub> is independently selected at each occurrence the group consisting of halogen, hydroxy, cyano, C<sub>1-4</sub>alkyl, -O(C<sub>1-4</sub>alkyl), -NH(C<sub>1-4</sub>alkyl), -N(C<sub>1-4</sub>alkyl)(C<sub>1-4</sub>alkyl), -S(O)<sub>n</sub>(alkyl) halo(C<sub>1-4</sub>)alkyl, halo(C<sub>1-4</sub>)alkoxy, CO(C<sub>1-4</sub>alkyl), CONH(C<sub>1-4</sub>alkyl), CON(C<sub>1-4</sub>alkyl)(C<sub>1-4</sub>alkyl), -XR<sub>A</sub>, and Y;

X is independently selected at each occurrence from the group consisting of -CH<sub>2</sub>-, -CHR<sub>B</sub>-, -O-, -C(=O)-, -C(=O)O-, -S(O)<sub>n</sub>-, -NH-, -NR<sub>B</sub>-, -C(=O)NH-, -C(=O)NR<sub>B</sub>-, -S(O)<sub>n</sub>NH-, -S(O)<sub>n</sub>NR<sub>B</sub>-, -OC(=S)S-, -NHC(=O)-, -NR<sub>B</sub>C(=O)-, -NHS(O)<sub>n</sub>-, -OSiH<sub>n</sub>(C<sub>1-4</sub>-alkyl<sub>2-n</sub>)-, and -NR<sub>B</sub>S(O)<sub>n</sub>-;

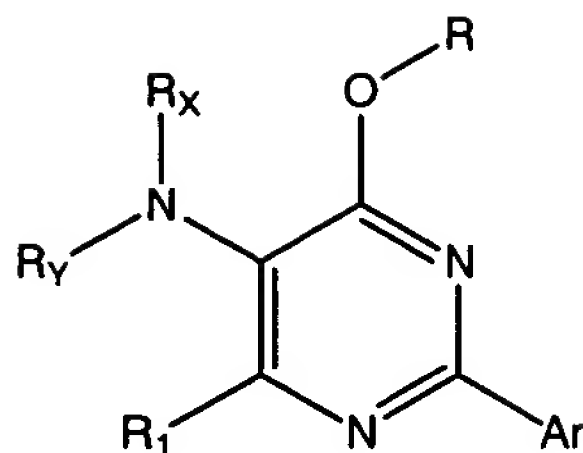
Y and Z are independently selected at each occurrence from the group consisting of: 3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, C<sub>1-4</sub>alkyl, -O(C<sub>1-4</sub>alkyl), -NH(C<sub>1-4</sub>alkyl), -N(C<sub>1-4</sub>alkyl)(C<sub>1-4</sub>alkyl), and -S(O)<sub>n</sub>(alkyl); and

n is 0, 1, or 2.

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17. (thrice amended) A compound or salt according to Claim 3 of Formula B:

*Sub E1*



FORMULA B

Ar is phenyl mono-, di-, or tri-substituted with  $R_C$ ;

R is selected from straight, branched, or cyclic alkyl groups, (cycloalkyl)alkyl groups, straight, branched, or cyclic alkenyl groups, or straight or branched alkynyl groups, and which are optionally substituted by one or more substituents independently chosen from oxo, hydroxy, halogen, cyano,  $-O(C_{1-4} \text{ alkyl})$ , amino,  $-NH(C_{1-4} \text{ alkyl})$ , and  $-N(C_{1-4} \text{ alkyl})(C_{1-4} \text{ alkyl})$ ;

$R_1$  is selected from hydrogen, halogen, cyano,  $C_{1-4}$  alkyl,  $(C_{3-7} \text{ cycloalkyl})C_{1-4} \text{ alkyl}$ , halo( $C_{1-4}$  alkyl), halo( $C_{1-4}$ )alkoxy, and  $-O(C_{1-4} \text{ alkyl})$ ; and

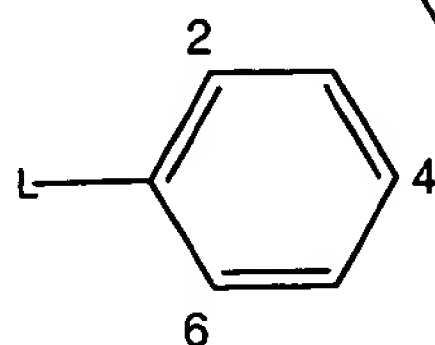
$R_X$  and  $R_Y$  are the same or different and are independently selected from:

- hydrogen,
- $-(C=O)alkyl_A$ , wherein  $alkyl_A$  is a straight or branched alkyl group having from 1 to 8 carbon atoms;
- straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, (cycloalkyl)alkyl groups consisting of 4 to 11 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms, each of which may be further substituted with one or more substituent(s) independently selected from (i) hydroxy, halogen, amino, cyano,  $-O(C_{1-4} \text{ alkyl})$ ,  $-NH(C_{1-4} \text{ alkyl})$ , and  $-NH(C_{1-4} \text{ alkyl})(C_{1-4} \text{ alkyl})$ , and (ii) 3- to 7-membered carbocyclic and heterocyclic groups, which are saturated, unsaturated, or aromatic, which may be substituted with one or more substituents selected from halogen, halo( $C_{1-4}$ )alkyl, halo( $C_{1-4}$ )alkoxy, oxo, hydroxy, amino,  $C_{1-4}$  alkyl,  $-O(C_{1-4} \text{ alkyl})$ ,  $-NH(C_{1-4} \text{ alkyl})$ ,  $-N(C_{1-4} \text{ alkyl})(C_{1-4} \text{ alkyl})$ , and  $-S(O)_n(alkyl)$ , wherein said 3- to 7-membered heterocyclic groups

D/S  
El

contain one or more heteroatom(s) independently selected from N, O, and S, with the point of attachment being either carbon or nitrogen.

19. (thrice amended) A compound or salt according to Claim 17, wherein Ar is a phenyl group of the formula:



wherein L indicates a bond to the pyrimidine ring in Formula B

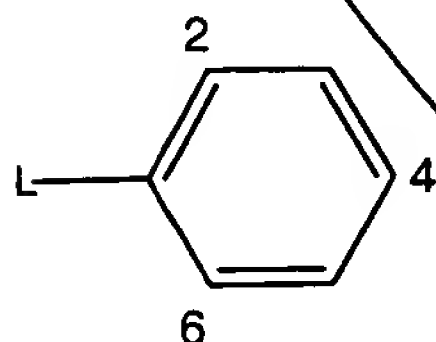
and the Ar phenyl group is substituted at one, two, or three of positions 2, 4, and 6 with substituents independently selected from:

- D/G
- S/h  
El
- halogen, cyano, halo(C<sub>1-4</sub>)alkyl, halo(C<sub>1-4</sub>)alkoxy, hydroxy, amino, C<sub>1-6</sub> alkyl, C<sub>1-6</sub>alkoxy, (C<sub>1-4</sub>alkoxy)C<sub>1-4</sub>alkoxy, and mono- or di(C<sub>1-4</sub>alkyl)amino,
  - C<sub>1-6</sub> alkyl and C<sub>1-6</sub>alkoxy which are further substituted with a 3- to 7-membered carbocyclic and heterocyclic group, which is saturated, unsaturated, or aromatic, which 3- to 7-membered carbocyclic and heterocyclic group may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, C<sub>1-4</sub>alkyl, -O(C<sub>1-4</sub>alkyl), -NH(C<sub>1-4</sub>alkyl), and -N(C<sub>1-4</sub>alkyl)(C<sub>1-4</sub>alkyl);

R<sub>X</sub> and R<sub>Y</sub> are the same or different and are independently selected from the group consisting of:

- hydrogen (with the proviso that R<sub>X</sub> and R<sub>Y</sub> are not both hydrogen),
- (C=O)alkyl<sub>A</sub>, wherein alkyl<sub>A</sub> is a straight or branched alkyl group having from 1 to 8 carbon atoms;
- straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, (cycloalkyl)alkyl groups consisting of 4 to 11 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms, which may be further substituted with one or more substituent(s) independently selected from hydroxy, halogen, amino, cyano, -O(C<sub>1-4</sub>alkyl), -NH(C<sub>1-4</sub>alkyl), and -NH(C<sub>1-4</sub>alkyl)(C<sub>1-4</sub>alkyl).

20. (thrice amended) A compound or salt according to Claim 17, wherein  
Ar is a phenyl group of the formula:



wherein L indicates a bond to the pyrimidine ring in Formula B

and the Ar phenyl group is substituted at one, two, or three of positions 2, 4, and 6 with  
substituents independently selected from:

- i) halogen, cyano, halo(C<sub>1-4</sub>)alkyl, halo(C<sub>1-4</sub>)alkoxy, hydroxy, amino, C<sub>1-6</sub> alkyl, C<sub>1-6</sub>alkoxy, (C<sub>1-4</sub>alkoxy)C<sub>1-4</sub>alkoxy, and mono- or di(C<sub>1-4</sub>alkyl)amino,
- ii) C<sub>1-6</sub> alkyl and C<sub>1-6</sub>alkoxy which are further substituted with a 3- to 7-membered carbocyclic and heterocyclic group, which is saturated, unsaturated, or aromatic, which 3- to 7-membered carbocyclic and heterocyclic group may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, C<sub>1-4</sub>alkyl, -O(C<sub>1-4</sub>alkyl), -NH(C<sub>1-4</sub>alkyl), and -N(C<sub>1-4</sub>alkyl)(C<sub>1-4</sub>alkyl);

R<sub>X</sub> and R<sub>Y</sub> are the same or different and are independently selected from the group consisting of:

- a) hydrogen (with the proviso that R<sub>X</sub> and R<sub>Y</sub> are not both hydrogen),
- b) -(C=O)alkyl<sub>A</sub>, wherein alkyl<sub>A</sub> is a straight or branched alkyl group having from 1 to 8 carbon atoms;
- c) straight, branched, or cyclic alkyl groups consisting of 1 to 8 carbon atoms, (cycloalkyl)alkyl groups consisting of 4 to 11 carbon atoms, straight, branched, or cyclic alkenyl groups consisting of 2 to 8 carbon atoms, or straight or branched alkynyl groups consisting of 2 to 8 carbon atoms.

## REMARKS

The Applicants appreciate the Examiner's thorough examination of the subject application, the indication that claims 4, 22, and 24-68 would be in a condition for allowance if